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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,669	11/27/2001	Ann-Kristin Karlsson	06275-160002	1605

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EXAMINER	
MAIER, LEIGH C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,669	KARLSSON ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *65-144* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *65-144* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-64 have been canceled. Claims 65-144 have been added and are pending. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Any objection or rejection not expressly repeated has been withdrawn. The arguments filed December 3, 2004 will be addressed insofar as they apply to the new grounds of rejection set forth below.

Claim Objections

Claims 66 and 85 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form. Both these claims and the claims from which they depend require that at least 98.5% of the powder composition be pure budesonide.

Claim Rejections - 35 USC § 112 – 2nd paragraph

Claim 104 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim contains the trademark/trade names Tyloxapol™ and Tween™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second

paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe particular surfactants and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

Claims 65-70, 73-80, and 84-93 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAKUPOVIC et al (WO 96/32095) in view of RUBINFELD et al (US 5,824,668) and ANSEL et al (Pharmaceutical Dosage Forms and Drug delivery Systems, 1995).

The invention is as described in previous Office actions. Regarding claims 65 and 84, claim 65 recites a "sterile powder," and claim 84 recites a "sterilized powder." It is possible that these could be different in scope, in that the former could have been prepared under sterile conditions from sterile reactants, so that the final product is sterile without this product itself having undergone sterilization. However, the specification does not describe such a process, so for the purposes of the present prosecution, "sterile powder" is considered to be the same as "sterilized powder."

Claims 88-93 are product-by-process claims. However, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a

product of the prior art, the claim is unpatentable even though the prior product was made by a different process.

JAKUPOVIC teaches a crystalline form of budesonide, in which 90% of the particles have a diameter of less than 5.7 μm, for nasal inhalation in treating diseases of the respiratory tract. See example 1, page 8 and page 4, lines 4-6. The reference further teaches a particle range of about 0.1 μm to about 10 μm. See paragraph bridging pages 3 and 4. The reference further teaches the preparation of pharmaceutical compositions by adding any of a variety of pharmaceutically acceptable carriers. See page 5, beginning line 11, continuing through page 6, line 17. JAKUPOVIC does not teach a sterile product.

RUBINFELD discloses steroid products and teaches that they may be sterilized in the form of a powder by ethylene oxide gas, or alternatively in solution by filtration followed by isolation under sterile conditions. See col 14, lines 11-24. ANSEL demonstrates that these processes are well known in the art and would be fully enabled. See pages 294-298.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to sterilize the respirable, dry powders disclosed by JAKUPOVIC by either treatment with ethylene oxide or filtration of the product in solution before precipitation as described in the JAKUPOVIC process. The artisan would have been motivated to sterilize the respirable particles, to prevent microbial growth in the packaged material meant for administration to patients, with a reasonable expectation of success. It is noted that the filter size recommended by JAKUPOVIC would not be adequate for sterilization. However, the reference does not disclose filter size as a variable that controls particle size. See page 4, lines 14-19.

Therefore it would be obvious to use a smaller filter and conduct the balance of the process under sterile conditions to obtain a sterile product.

It would also be obvious to the ordinarily skilled worker to purify the glucocorticosteroid (prepare in a form having a high percentage of the glucocorticosteroid by weight) in order to limit contaminants in products for human administration.

It appears that it is Applicant's position that the use of ethylene oxide for sterilization is not compatible with the preparation of a pharmaceutically acceptable product. The teachings of RUBINFELD and ANSEL, which are specifically directed to the preparation of pharmaceutically acceptable products, contradict this.

Claims 65-93 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAKUPOVIC et al (WO 96/32095) in view of RUBINFELD et al (US 5,824,668) and ANSEL et al (Pharmaceutical Dosage Forms and Drug delivery Systems, 1995) and further in view of RADHAKRISHNAN et al (US 5,192,528).

The invention is as set forth above. Claims 71, 72, and 81-83 recite products having a significant percentage of particle sizes less or equal to about 5 μm.

JAKUPOVIC teaches as set forth above. The aim of the reference is preparation of glucocorticosteroids available to the respiratory tract including the lower area. See page 1, lines 9-15. As noted above, JAKUPOVIC teaches the range of particles of about 0.1 μm to about 10 μm, but the reference does not specifically exemplify particles of less than 5 μm. However, the reference teaches how the size of the particles may be controlled by process parameters that one of ordinary skill would be able to optimize with routine experimentation.

RUBINFELD and ANSEL teach as set forth above.

RADHAKRISHNAN teaches that corticosteroids, including budesonide, have utility for the treatment of a variety of respiratory disorders. See col 1-2 and col 7, lines 57-63. The reference further teaches that aerosol particles of corticosteroid formulations will be directed to particular sites in the respiratory tract, depending on their size. Particles must be must be less than about 1 μm in order to reach the lower region of the respiratory tract (alveoli). See figure 1 and col 5, lines 37-48.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare glucocorticosteroid in the form of sterile, respirable particles with MMD of less than 1 μm. The artisan would have been motivated to prepare this size in order for the respirable glucocorticosteroid to reach the alveoli during treatment. The artisan would reasonably expect success in preparing such particles, as JAKUPOVIC had taught how to prepare particles down to about 0.1 μm. The artisan would be motivated to sterilize the product for reasons described above. Purity limitations are addressed above.

Claims 65-70, 73-80, 84-109, 112-117, 121-123, 127-131, 136-138, and 142-144 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAKUPOVIC et al (WO 96/32095) in view of RUBINFELD et al (US 5,824,668) and ANSEL et al (Pharmaceutical Dosage Forms and Drug delivery Systems, 1995) and further in view of HELZNER (WO 97/01341).

The invention is as set forth above. Dependents are drawn to suspensions comprising the product of the independent claims and therapeutic methods comprising administration of either the powder or the suspension.

JAKUPOVIC teaches as set forth above. The reference teaches treatment of diseases of the respiratory tract in general, but not the particular disorders recited in the claims. The reference teaches the preparation of pharmaceutical compositions, but not specifically suspensions.

RUBINFELD and ANSEL teach as set forth above.

HELZNER teaches the preparation of suspensions comprising anti-inflammatory corticosteroids, including budesonide. See abstract and pp 5-8. The reference teaches the addition of a variety of typical pharmaceutical additives, such as those recited in the claims. The reference teaches a preferred pH range of about 4.0 to 6.5. The reference further teaches that these compounds have utility in the treatment of allergic rhinitis.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a sterile suspension comprising the budesonide and having a pH in the recited ranges. The artisan would be motivated to prepare such a suspension for the art-disclosed utility. It would be within the scope of the artisan to select appropriate additives and optimize their concentration through routine optimization.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use the dry, sterile glucocorticosteroids or as aqueous suspensions of said glucocorticosteroids for the treatment of the recited respiratory disorders, inflammation, allergies or rhinitis. It would be within the scope of the artisan to optimize the dosage and prepare suspensions of appropriate concentration for said dosage through routine experimentation.

Claims 65-70, 73-80, 84-117, 121-123, 127-131, 136-138, and 142-144 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAKUPOVIC et al (WO 96/32095) in view of RUBINFELD et al (US 5,824,668) and ANSEL et al (Pharmaceutical Dosage Forms and Drug delivery Systems, 1995) and further in view of HELZNER (WO 97/01341) and GUY et al (US 5,540,930).

The invention is as set forth above. Claims 110 and 111 require that the suspension comprise EDTA.

JAKUPOVIC, RUBINFELD, and ANSEL, teach as set forth above.

HELZNER teaches as set forth above. The reference teaches a variety of additives, including benzalkonium chloride. The reference does not teach a suspension comprising EDTA.

GUY teaches that EDTA—alone or in combination with benzalkonium chloride—has utility in preventing microbial contamination of corticosteroid suspensions. See col 3, lines 35-40; col 4, lines 1-14; and col 5, lines 1-5.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a sterile suspension comprising budesonide as set forth above. It would be further obvious to prepare one comprising EDTA for its utility as an antimicrobial to protect the sterile composition from microbial contamination.

Claims 65-70, 73-80, 84-95, 115-120, 124-126, 130-132, and 139-141 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAKUPOVIC et al (WO 96/32095) in view of RUBINFELD et al (US 5,824,668) and ANSEL et al (Pharmaceutical Dosage Forms and Drug delivery Systems, 1995) in further view of BRATTSAND et al (US 3,992,534).

The invention is as set forth above. Dependents are drawn to suspensions comprising the product of the independent claims and therapeutic methods comprising administration of either the powder or the suspension.

JAKUPOVIC, RUBINFELD, and ANSEL, teach as set forth above. The references do not teach the treatment of COPD or asthma.

BRATTSAND teaches that budesonide (compound 12) has utility for the treatment of inflammatory conditions, asthma and obstructive lung disease. See col 12. The reference further teaches the preparation of budesonide in a variety of forms, including suspensions. See composition 8.

It would have been obvious to one having ordinary skill at the time the invention was made to prepare budesonide, in the form of a sterile powder or suspension, as set forth above. One of ordinary skill would be motivated to prepare such a composition for administration to a patient for the treatment of inflammatory disorders, asthma, or obstructive lung disease, such as COPD. The artisan would reasonably expect success in doing so because BRATTSAND had taught that budesonide has this utility.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 94-100 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,686,346 in view of RUBINFELD et al (US 5,824,668) and ANSEL et al (Pharmaceutical Dosage Forms and Drug delivery Systems, 1995). Claims 101, 102, 105, and 107-109 are rejected over claim 22. Claims 136-138 and 142-144 are rejected over claim 12.

Claims 1, 12, and 22 of '346 recites a suspension (or administration of said suspension) comprising budesonide suspended in an aqueous medium. The claim does not require that the suspension be sterile. However, it would be obvious to prepare the suspension in sterile form for reasons set forth above. One of ordinary skill would reasonably expect success in preparing a sterile composition using the teachings of RUBINFELD and ANSEL, as discussed above.

Claims 94-101 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 2 of U.S. Patent No. 6,291,445 in view of RUBINFELD et al (US 5,824,668) and ANSEL et al (Pharmaceutical Dosage Forms and Drug delivery Systems, 1995). Claims 136-138 and 142-144 are rejected over claim 8.

Claims 2 and 8 of '346 recites a suspension (or administration of said suspension) comprising budesonide suspended in an aqueous medium. The claim does not require that the suspension be sterile. However, it would be obvious to prepare the suspension in sterile form for

reasons set forth above. One of ordinary skill would reasonably expect success in preparing a sterile composition using the teachings of RUBINFELD and ANSEL, as discussed above.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Wednesday, or Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (571) 272-0661, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 872-9306.

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Leigh C. Maier

Leigh C. Maier
Primary Examiner
February 18, 2005